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Regioselective Palladium-Catalyzed Decarboxylative Cross-Coupling Reaction of Alkenyl Acids with Coumarins: Synthesis of 3-Styrylcoumarin Compounds

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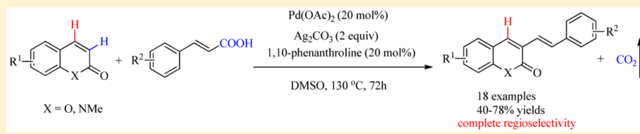
Supporting Information

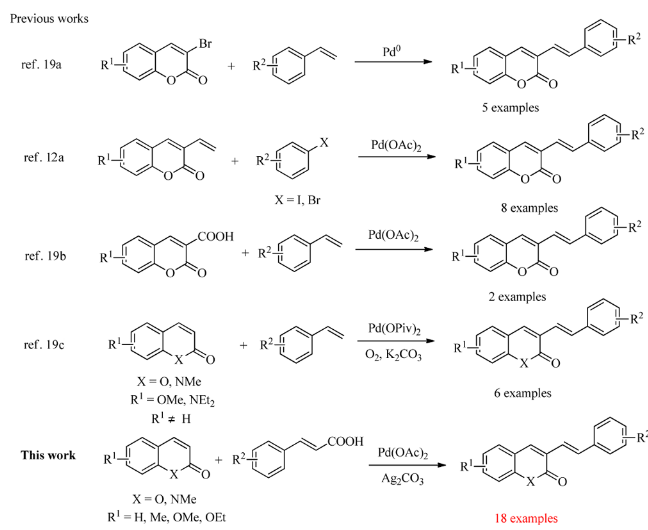
ABSTRACT: A novel and efficient protocol for the regioselective synthesis of 3-styrylcoumarins from readily available cinnamic acids and coumarins is presented. The reaction proceeds via a decarboxylative cross-coupling mediated by a catalytic amount of $Pd(OAc)_2$, with Ag_2CO_3 as an oxidant, and with 1,10-phenanthroline as a ligand. A plausible reaction mechanism for this process is depicted, and the resulting 3-styrylcoumarins show excellent fluorescence quantum yields.



Decarboxylative coupling reactions have become a powerful tool for regioselective C−C and C−heteroatom bond formation,[1] thus providing new protocols for Heck-type reactions,[2] oxidative arylations,[3] redox-neutral cross-coupling reactions,[4] and allylations.[5] Among these, alkenyl acids act as cross-coupling components by a metal-promoted decarboxylation process and are used in construction of C−C,[6] C−N,[7] C−S,[8] and C−P[9] bonds because of their stability, low cost, diversity, ready availability, and nontoxic byproduct (CO_2). From environmental and economic perspectives, the development of organic synthesis using an inexpensive and stable material such as alkenyl acids would be significantly important.

Coumarins constitute a major class of naturally occurring compounds, and privileged medicinal scaffolds have been extensively investigated with regard to their pharmacological activity[10] and outstanding optical properties.[11] Because of effective fluorophores characterized by high fluorescence quantum yields,[12] several coumarins have been shown to exhibit their photophysical properties.[13−18] The challenge is how to effectively increase the spectroscopic band intensity of coumarin derivatives. The best solution is extending the conjugated π-electron system, yielding coumarin derivatives with greater intensity. Recently, various synthetic approaches have been reported to synthesize 3-styrylcoumarins in the literature.[19] For example, Heck cross-coupling reactions between 3-bromocoumarin and olefins,[19a] 3-vinyl coumarins and aryl halides,[12a] coumarin-3-carboxylic acid and olefins,[19b] and coumarins and alkenes[19c] are a few prominent methods of synthesizing 3-styryl coumarins (Scheme 1). In light of the literature precedent[1−19] and continuation of our efforts in the development of transition metal-catalyzed C−H functionalization,[20] we thought it would be of interest to develop a method for a decarboxylative cross-coupling reaction of α,β-unsaturated carboxylic acids using coumarins. Herein, we disclose an efficient, economic route for rapid synthesis of 3-styrylcoumarins via palladium-catalyzed decarboxylative coupling of cinnamic acids employing coumarins.

Scheme 1. Reported Methods for the Synthesis of 3-Styrylcoumarins



Our initial experiments showed that using a $Pd(OAc)_2$/AgOAc/DMSO catalytic system, the C3-olefination of coumarin occurred with complete regioselectivity giving a low isolated yield (10%) (Table 1, entry 1). Addition of 20 mol % 1,10-phenanthroline increased the yield to 40% (Table 1, entry 2). In the presence of 1,10-phenanthroline, a series of palladium catalysts were screened and did not display better catalytic activity except $PdCl_2$ showing activity similar to that of $Pd(OAc)_2$ (Table 1, entries 3−5; Table S1, Supporting

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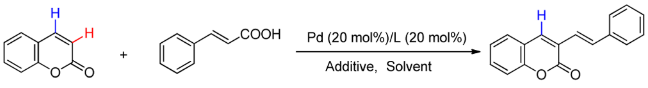
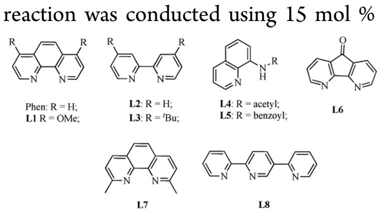
Table 1. Optimization of Reaction Conditions[a]



1a 2a 3aa

entry	catalyst	ligand	additive[b]	solvent	yield (%)[c]
1	$Pd(OAc)_2$	–	AgOAc	DMSO	10
2	$Pd(OAc)_2$	Phen	AgOAc	DMSO	40
3	$PdCl_2$	Phen	AgOAc	DMSO	36
4	$Pd(acac)_2$	Phen	AgOAc	DMSO	30
5	$Pd(dba)_2$	Phen	AgOAc	DMSO	22
6	$Pd(OAc)_2$	Phen	Ag_2CO_3	DMSO	47
7	$Pd(OAc)_2$	Phen	Ag_2O	DMSO	42
8	$Pd(OAc)_2$	Phen	AgOTf	DMSO	39
9	$Pd(OAc)_2$	**L1**	Ag_2CO_3	DMSO	32
10	$Pd(OAc)_2$	**L2**	Ag_2CO_3	DMSO	17
11	$Pd(OAc)_2$	**L3**	Ag_2CO_3	DMSO	12
12	$Pd(OAc)_2$	**L4**	Ag_2CO_3	DMSO	14
13	$Pd(OAc)_2$	**L5**	Ag_2CO_3	DMSO	11
14	$Pd(OAc)_2$	**L6**	Ag_2CO_3	DMSO	15
15	$Pd(OAc)_2$	**L7**	Ag_2CO_3	DMSO	34
16	$Pd(OAc)_2$	**L8**	Ag_2CO_3	DMSO	41
17	$Pd(OAc)_2$	Phen	Ag_2CO_3	PhCl	14
18	$Pd(OAc)_2$	Phen	Ag_2CO_3	DMF	31
19	$Pd(OAc)_2$	Phen	Ag_2CO_3	dioxane	0
20	$Pd(OAc)_2$	Phen	Ag_2CO_3	DCE	0
21	$Pd(OAc)_2$	Phen	Ag_2CO_3	CH_3CN	0
22[d]	$Pd(OAc)_2$	Phen	Ag_2CO_3	DMSO	69
23[e]	$Pd(OAc)_2$	Phen	Ag_2CO_3	DMSO	70
24[f]	$Pd(OAc)_2$	Phen	Ag_2CO_3	DMSO	43

[a]All reactions were conducted under the following conditions: coumarin **1a** (0.3 mmol), **2a** (0.2 mmol), Pd catalyst (20 mol %), and ligand (20 mol %) in different solvents (2 mL) at 130 °C for 72 h. [b]Amount of 2.0 equiv. [c]Isolated yield based on **2a**. [d]Sealed tube. [e]At 140 °C. [f]The reaction was conducted using 15 mol % $Pd(OAc)_2$.

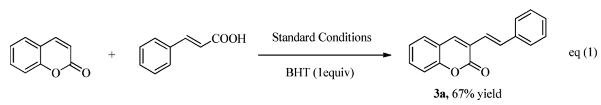


Information). Among the additives examined, Ag_2CO_3 provided the best result (Table 1, entries 6–8; Table S1, Supporting Information). Some other N,N-ligands **L1–L8** were also evaluated; while these ligands did produce active catalyst systems, the yields were inferior to that obtained with 1,10-phenanthroline (Table 1, entries 9–16; Table S2, Supporting Information). The solvent also affected the coupling reaction of coumarin and alkenyl acid. No product was found with dioxane, DCE, or CH_3CN as solvent, and only poor yields were obtained when other solvents such as PhCl and DMF were employed (Table 1, entries 17–21), where DMSO turned out to be the most appropriate (Table S3, Supporting Information). When in the sealed tube, the yield of **3a** was enhanced from 40 to 69% (Table 1, entry 22), but no obvious improvement in the yield could be obtained as the temperature was increased to 140 °C (Table 1, entry 22 vs entry 23). A very slow reaction rate and low yield were observed when the catalytic amount of $Pd(OAc)_2$ decreased from 20 to 15 mol % (Table 1, entry 22 vs entry 24). The investigations described above revealed that the $Pd(OAc)_2$/Ag_2CO_3/phen/DMSO system is the best combination for promoting the olefination.

With the optimized reaction conditions established, we started to investigate the scope and limitation of this reaction, and the results are summarized in Table 2. It was observed that a range of selected coumarin derivatives and cinnamic acids were compatible with the reaction conditions, resulting in the formation of the desired products in moderate to good yields with complete regioselectivity. Cinnamic acids featuring electron-donating or neutral groups at the phenyl ring provided somewhat higher yields of the olefination products than did those bearing electron-withdrawing groups (**3a** and **3b** vs **3c** and **3d** and **3e** and **3g** vs **3h** and **3i**). Gratifyingly, moderate to good reaction yields (55–78%) were obtained when courmarins were substituted with electron-donating groups such as -Me, -OMe, and -OEt at the C6 or C7 position even in a shorter time (**3e–o**). The crystallization of compound **3g** from ethanol gave a single crystal suitable for X-ray analysis. It illustrates the molecular structure of the substituted 3-styrylcoumarin **3g** (see page S29 of the Suporting Information). Unfortunately, coumarin possessing an electron-withdrawing group such as $-NO_2$ at the C6 position gave the desired product **3p** in poor yield. The electron-withdrawing group presumably is not conducive to the formation of intermediate **II** (see Scheme 3). We further investigated additional substrates and were pleased to observe that quinolinones also worked well in the optimized system, leading to the formation of **3q** and **3r**.

To investigate the reaction mechanism, a control experiment was conducted (Scheme 2). A 67% yield of **3a** was smoothly obtained in the presence of the radical scavenger butyleret hydroxytoluene (BHT) (eq 1), which could indicate that free radical pathway is not involved. On the basis of these data, we proposed a mechanism for the present reaction pathway (Scheme 3).[21] Electrophilic palladation of coumarin at the C3 position with the Pd ligand species was favorable because of the more nucleophilic 3 position, thereby affording intermediate **II**.

Scheme 2. Mechanistic Investigations of the Decarboxylative Cross-Coupling Reaction



Scheme 3. Plausible Mechanism

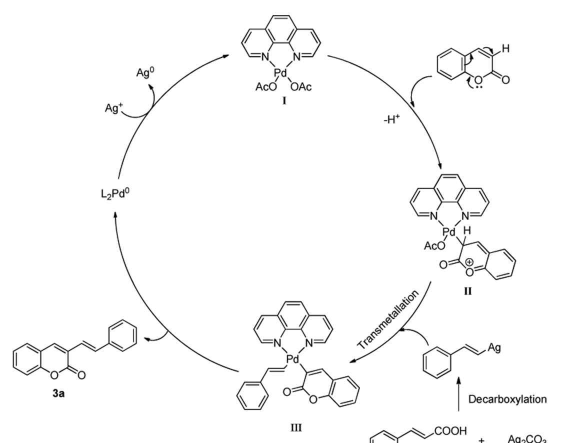


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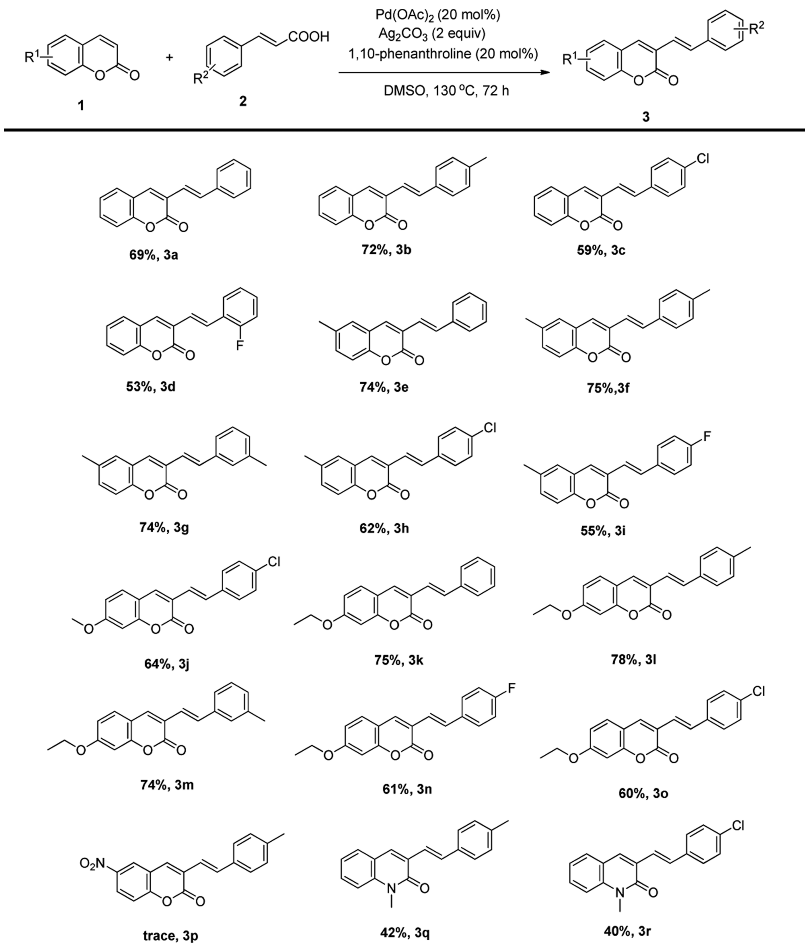
Table 2. Direct C3-Olefination of the Coumarins with Various Cinnamic Acid Derivatives[a,b]



[a]Reaction conditions: **1** (0.3 mmol), **2** (0.2 mmol), $Pd(OAc)_2$ (20 mol % to **2**), Ag_2CO_3 (2 equiv to **2**), 1,10-phenanthroline (20 mol % to **2**), DMSO (2 mL), at 130 °C, sealed tube, 72 h. [b]Average isolated yield based on **2**.

In parallel, the silver-mediated decarboxylation of cinnamic acid **1a** affords alkenyl-silver species. Alkenyl-silver would then transfer the alkenyl group to intermediate **II** during the formation of silver derivatives by transmetalation to give intermediate **III**. Finally, the desired product **3a** would be released, regenerating the initial palladation species and resuming the catalytic cycle.

Absorption and emission properties as well as fluorescence quantum yields (Φ_F) of the synthesized coumarin derivatives **3** are summarized in Table 3. A change of <8 nm in λ_{max} was observed among **3e–i** by simply modifying the substituents at the benzene ring moiety position (Table 3, entries 5–9, respectively). In comparison with those of **3a** and **3b**, a longer wavelength of the absorption maximum peak (λ_{max}) was obtained upon the introduction of electron-donating groups such as ethoxy at the C7 position (Table 3, entry 3 vs entry 1 and entry 4 vs entry 2). All of these compounds exhibited excellent fluorescence, regardless of the electron-donating or -withdrawing ability of the substituents. The fluorescence quantum yield (Φ_F) remained in the range of 0.39–0.92. Obviously, the introduction of electron-donating groups into 3-styrylcoumarin derivatives produced fluorescence quantum yields better than those with electron-withdrawing groups.

Table 3. Photophysical Properties of 3-Styrylcoumarin Derivatives 3

entry	compound	λ_{max}[a] (nm)	λ_{em}[b] (nm)	Φ_F[c]
1	**3a**	349	440	0.67
2	**3b**	354	447	0.76
3	**3k**	358	444	0.83
4	**3l**	365	452	0.92
5	**3e**	349	444	0.81
6	**3f**	354	448	0.88
7	**3g**	351	443	0.87
8	**3h**	354	440	0.39
9	**3i**	346	442	0.52
10	**3j**	346	450	0.79
11	**3m**	355	446	0.86
12	**3n**	360	442	0.82
13	**3o**	350	443	0.75

[a]Absorption maxima in acetonitrile (longest wavelength transition). [b]Maxima of the corrected emission spectra in acetonitrile. [c]Determined by quinine sulfate (Φ_F = 0.55; excited at 347 nm) as a standard.

In summary, we have successfully developed a flexible and rapid route for synthesizing a series of 3-styryl coumarins from cinnamic acids and coumarins via a palladium-catalyzed decarboxylative cross-coupling reaction. 3-Styrylcoumarins were obtained in moderate to good yields and showed good fluorescence quantums. This study provides a clue about the further development of new types of fluorescent materials.

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■ EXPERIMENTAL SECTION

The reaction mixture of coumarins **1** (0.3 mmol), alkenyl acid **2** (0.2 mmol), $Pd(OAc)_2$ (20 mol %), Ag_2CO_3 (2 equiv), 1,10-phenanthroline (20 mol %), and DMSO (2 mL) was stirred at 130 °C for 72 h in a sealed tube and monitored periodically by TLC. Upon completion of the reaction, the mixture was diluted with water (30 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with water and brine, dried over Na_2SO_4, and filtered. The solvent was removed under vacuum. The residue was purified by flash column chromatography to afford **3**.

3-Styrylchromen-2-one (3a). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 69% (34.2 mg) as a yellow solid: mp 161−163 °C (lit.[12a] 162−164 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.63 (d, *J* = 16.3 Hz, 1H), 7.58−7.50 (m, 4H), 7.41−7.30 (m, 5H), 7.16 (d, *J* = 16.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 152.8, 136.8, 133.6, 131.1, 128.7, 128.4, 127.6, 127.0, 124.9, 124.5, 122.0, 119.7, 116.4; HRAPCIMS calcd for $C_{17}H_{12}O_2$ $(M + H)^+$ 249.0916, found 249.0908.

3-(2-*p*-Tolylvinyl)chromen-2-one (3b). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 72% (37.7 mg) as a yellow solid: mp 147−149 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.49 (d, *J* = 16.3 Hz, 1H), 7.45−7.29 (m, 4H), 7.26−7.18 (m, 2H), 7.10 (d, *J* = 7.8 Hz, 2H), 7.02 (d, *J* = 16.3 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 152.7, 138.5, 136.2, 134.0, 133.6, 130.9, 129.5, 127.5, 126.9, 125.1, 124.5, 121.0, 119.7, 116.4, 21.3; HRAPCIMS calcd for $C_{18}H_{14}O_2$ $(M + H)^+$ 263.1072, found 263.1067.

3-[2-(4-Chlorophenyl)vinyl]chromen-2-one (3c). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 59% (33.2 mg) as a yellow solid: mp 154−156 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.61 (d, *J* = 16.5 Hz, 1H), 7.56−7.45 (m, 4H), 7.37−7.28 (m, 4H), 7.11 (d, *J* = 16.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 152.9, 137.3, 135.4, 134.1, 132.4, 131.3, 129.0, 128.1, 127.7, 124.7, 124.6, 122.7, 119.6, 116.5; HRAPCIMS calcd for $C_{17}H_{11}ClO_2$ $(M + H)^+$ 283.0526, found 283.0523.

3-[2-(4-Fluorophenyl)vinyl]chromen-2-one (3d). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 53% (28.2 mg) as a yellow solid: mp 145−148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.70 (d, *J* = 16.5 Hz, 1H), 7.65−7.61 (m, 1H), 7.54−7.48 (m, 2H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.31−7.26 (m, 2H), 7.25−7.19 (m, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.10−7.05 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5 [d, $J_{(C-F)}$ = 256.8 Hz], 160.4, 153.0, 137.1, 131.3, 129.8 [d, $J_{(C-F)}$ = 8.5 Hz], 127.7 [d, $J_{(C-F)}$ = 3.3 Hz], 127.5, 125.8 [d, $J_{(C-F)}$ = 3.7 Hz], 125.0, 124.8 [d, $J_{(C-F)}$ = 11.7 Hz], 124.6, 124.4 (d, *J* = 3.5 Hz), 124.2 [d, $J_{(C-F)}$ = 5.3 Hz], 119.6, 116.5, 115.9 [d, $J_{(C-F)}$ = 22.0 Hz]; HRAPCIMS calcd for $C_{17}H_{11}FO_2$ $(M + H)^+$ 267.0821, found 267.0813.

6-Methyl-3-styrylchromen-2-one (3e). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 74% (38.7 mg) as a yellow solid: mp 140−142 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.62 (d, *J* = 16.4 Hz, 1H), 7.59−7.55 (m, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.33−7.24 (m, 4H), 7.16 (d, *J* = 16.3 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.6, 151.0, 136.9, 134.2, 133.5, 132.2, 130.3, 128.8, 128.4, 127.5, 127.0, 124.8, 122.2, 119.5, 116.2, 20.8; HRAPCIMS calcd for $C_{18}H_{14}O_2$ $(M + H)^+$ 263.1072, found 263.1067.

6-Methyl-3-(2-*p*-tolylvinyl)chromen-2-one (3f). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 75% (41.4 mg) as a yellow solid: mp 172−174 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.57 (d, *J* = 16.4 Hz, 1H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.31−7.28 (m, 2H), 7.24−7.19 (m, 3H), 7.11 (d, *J* = 16.3 Hz, 1H), 2.43 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 1510, 138.5, 136.4, 134.2, 132,1, 133.4, 132.1, 129.5 127.4, 126.9, 125.0, 121.2, 119.5, 116.1, 21.4, 20.8; HRAPCIMS calcd for $C_{19}H_{16}O_2$ $(M + H)^+$ 277.1229, found 277.1224.

6-Methyl-3-(2-*m*-tolylvinyl)chromen-2-one (3g). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 74% (41.4 mg) as a yellow solid: mp 144−145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.58 (d, *J* = 16.3 Hz, 1H), 7.41−7.36 (m, 2H), 7.32−7.25 (m, 4H), 7.18−7.13 (m, 2H), 2.44 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 151.0, 138.3, 136.8, 136.6, 134.2, 133.5, 132.2, 129.3, 128.6, 127.6, 127.4, 124.9, 124.2, 121.9, 119.5, 116.1, 21.4, 20.8; HRAPCIMS calcd for $C_{19}H_{16}O_2$ $(M + H)^+$ 277.1229, found 277.1225.

3-[2-(4-Chlorophenyl)vinyl]-6-methylchromen-2-one (3h). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 62% (36.7 mg) as a yellow solid: mp 164−166 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.59 (d, *J* = 16.3 Hz, 1H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.32 (dd, *J* = 24.8, 9.4 Hz, 4H), 7.24 (d, *J* = 8.3 Hz, 1H), 7.09 (d, *J* = 16.3 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 151.0, 137.4, 135.4, 134.3, 134.0, 132.4, 132.2, 128.9, 128.1, 127.5, 124.5, 122.9, 119.3, 116.2, 20.8; HRAPCIMS calcd for $C_{18}H_{13}ClO_2$ $(M + H)^+$ 297.0682, found 297.0680.

3-[2-(4-Fluorophenyl)vinyl]-6-methylchromen-2-one (3i). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 55% (30.8 mg) as a yellow solid: mp 144−145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.57 (d, *J* = 16.3 Hz, 1H), 7.51 (dd, *J* = 8.1, 5.6 Hz, 2H), 7.30 (d, *J* = 8.7 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 1H), 7.05 (dd, *J* = 10.9, 6.1 Hz, 3H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.8 [d, $J_{(C-F)}$ = 247.0 Hz], 160.6, 151.0, 137.0, 134.2, 133.1 [d, $J_{(C-F)}$ = 3.7 Hz], 132.3, 131.4, 128.6 [d, $J_{(C-F)}$ = 8.0 Hz], 127.4, 124.6, 122.1, 119.4, 116.2, 115.8 [d, $J_{(C-F)}$ = 21.6 Hz], 20.8; HRAPCIMS calcd for $C_{18}H_{13}FO_2$ $(M + H)^+$ 281.0978, found 281.0976.

3-[2-(4-Chlorophenyl)vinyl]-7-methoxychromen-2-one (3j). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 64% (39.9 mg) as a yellow solid: mp 179−181 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.52 (d, *J* = 16.4 Hz, 1H), 7.44−7.40 (m, 3H), 7.32 (d, *J* = 8.5 Hz, 2H), 7.05 (d, *J* = 16.3 Hz, 1H), 6.88−6.82 (m, 2H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.7, 160.5, 154.7, 137.8, 135.7, 133.8, 131.1, 128.9, 128.7, 128.0, 123.0, 121.3, 113.3, 113.1, 100.5, 55.8; HRAPCIMS calcd for $C_{18}H_{13}ClO_3$ $(M + H)^+$ 313.0631, found 313.0627.

7-Ethoxy-3-styrylchromen-2-one (3k). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 75% (43.8 mg) as a yellow solid: mp 147−148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.56−7.53 (m, 3H), 7.42−7.29 (m, 3H), 7.30 (d, *J* = 7.4 Hz, 1H), 7.11 (d, *J* = 16.4 Hz, 1H), 6.86 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.82 (d, *J* = 2.1 Hz, 1H), 4.10 (q, *J* = 7.0 Hz, 2H), 1.47 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.9, 160.7, 154.7, 137.3, 137.1, 132.2, 128.7, 128.6, 128.1, 126.8, 122.4, 121.4, 113.3, 113.2, 100.9, 64.2, 14.6; HRAPCIMS calcd for $C_{19}H_{16}O_3$ $(M + H)^+$ 293.1178, found 293.1171.

7-Ethoxy-3-styrylchromen-2-one (3l). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 78% (47.8 mg) as a yellow solid: mp 148−150 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.49 (d, *J* = 16.3 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 1H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.06 (d, *J* = 16.3 Hz, 1H), 6.84 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.81 (d, *J* = 2.4 Hz, 1H), 4.09 (q, *J* = 7.0 Hz, 2H), 2.36 (s, 3H), 1.46 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 160.8, 154.6, 138.2, 136.8, 134.3, 132.2, 129.5, 128.5, 126.8, 121.6, 121.3, 113.3, 113.2, 100.9, 64.2, 21.3, 14.6; HRAPCIMS calcd for $C_{20}H_{18}O_3$ $(M + H)^+$ 307.1334, found 307.1332.

7-Ethoxy-3-(2-*m*-tolylvinyl)chromen-2-one (3m). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 74% (45.2 mg) as a yellow solid: mp 138−140 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.51 (d, *J* = 16.3 Hz, 1H), 7.44−7.33 (m, 3H), 7.28 (d, *J* = 6.0 Hz, 1H), 7.12 (dd, *J* = 12.2, 4.0 Hz, 2H), 6.90−6.81 (m, 2H), 4.12 (q, *J* = 6.9 Hz, 2H), 2.40 (s, 3H), 1.49 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 160.8, 154.6, 138.3, 137.0, 132.3, 129.0, 128.6, 128.5, 127.5, 124.1, 122.1, 121.5, 113.3, 113.2, 100.9, 64.2, 21.4, 14.6; HRAPCIMS calcd for $C_{20}H_{18}O_3$ $(M + H)^+$ 307.1334, found 307.1331.

7-Ethoxy-3-[2-(4-fluorophenyl)vinyl]chromen-2-one (3n). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 61% (37.8 mg) as a yellow solid: mp 118−120 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.52−7.49 (m, 2H), 7.41 (d, *J* = 8.5 Hz, 1H), 7.08−6.99 (m, 3H), 6.91−6.77 (m, 3H), 4.11 (q, *J* = 6.9 Hz, 2H), 1.47 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ

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162.6 [d, $J_{(C-F)}$ = 246.6 Hz], 161.9, 154.6, 137.4, 133.3 [d, $J_{(C-F)}$ = 3.3 Hz], 131.0, 128.6, 128.3 [d, $J_{(C-F)}$ = 8.0 Hz], 122.2, 121.2, 115.7 [d, $J_{(C-F)}$ = 21.6 Hz], 113.3, 113.2, 108.9, 100.9, 64.2, 14.5; HRAPCIMS calcd for $C_{19}H_{15}FO_3$ $(M + H)^+$ 311.1083, found 311.1067.

3-[2-(4-Chlorophenyl)vinyl]-7-ethoxychromen-2-one (3o). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 60% (39.1 mg) as a yellow solid: mp 118−120 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.50 (d, *J* = 16.4 Hz, 1H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 1H), 7.31 (d, *J* = 8.5 Hz, 2H), 7.03 (d, *J* = 16.3 Hz, 1H), 6.84 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.80 (d, *J* = 2.3 Hz, 1H), 4.09 (q, *J* = 7.0 Hz, 2H), 1.45 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 160.6, 154.7, 137.8, 135.7, 133.7, 130.9, 128.9, 128.7, 127.9, 123.1, 121.1, 113.4, 113.1, 100.9, 64.2, 14.6; HRAPCIMS calcd for $C_{19}H_{15}ClO_3$ $(M + H)^+$ 327.0788, found 327.0782.

6-Nitro-3-(2-*p*-tolylvinyl)chromen-2-one (3p). HRAPCIMS calcd for $C_{18}H_{13}NO_4$ $(M + Na)^+$ 330.0742, found 330.0739.

1-Methyl-3-(2-*p*-tolylvinyl)-1*H*-quinolin-2-one (3q). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 42% (24.7 mg) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.56−7.45 (m, 4H), 7.40−7.34 (m, 2H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 2H), 3.79 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 139.0, 137.9, 134.8, 132.9, 131.7, 129.9, 129.4, 128.6, 128.2, 126.8, 122.5, 122.3, 120.9, 114.0, 29.9, 21.3; HRAPCIMS calcd for $C_{19}H_{17}NO$ $(M + H)^+$ 276.1388, found 276.1380.

3-[2-(4-Chlorophenyl)vinyl]-1-methyl-1*H*-quinolin-2-one (3r). Purified via flash column chromatography with 20% ethyl acetate/hexane, yielding 40% (23.6 mg) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.55−7.48 (m, 4H), 7.39−7.29 (m, 5H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 139.1, 136.0, 133.8, 133.5, 130.5, 130.3, 128.8, 128.,7, 128.4, 128.0, 124.3, 122.4, 120,7, 114.0, 29.7; HRAPCIMS calcd for $C_{18}H_{15}ClNO$ $(M + H)^+$ 296.0842, found 296.0834.

■ ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures and characterization of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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